

REMARKS

The Official Action dated April 10, 2002 has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claim 20 is amended as to a matter of form to clarify the method in accordance with the teachings of the specification. A Version With Markings Showing Changes Made is attached. Claims 21 and 22 are added. Support for claim 21 is found in the specification on page 1, lines 10-11. Support for claim 22 is found in the specification on page 3, lines 7-8. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

Claim 20 was rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential elements. Specifically, the Examiner asserted that claim 20 lacked a last step or phrase that states the accomplishment of the goals for the method, i.e. how a reduction in the formation of trisulfides in the production of recombinant peptides is achieved.

Accordingly, Applicants have amended claim 20 to include a step that accomplishes the goals for the method. Claim 20 now recites a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides, wherein a metal salt is added during or after fermentation, prior to peptide isolation. It is therefore submitted that the method defined by claim 20 is definite, and the rejection under 35 U.S.C. §112, second paragraph, has been overcome. Reconsideration is respectfully requested.

Claims 1-3, 5-8, and 11-20 were rejected under 35 U.S.C. §102(e) as being anticipated by Builder et al, U.S. Patent No. 5,663,304. The Examiner asserted that Builder et al teach a method for production of recombinant peptides comprising fermenting cells to produce recombinant peptides in the presence of metal salt prior to peptide isolation. Further, the Examiner asserted that Builder et al teach that the use of metals facilitate disulfide oxidation of polypeptides and yield correct refolding of a misfolded polypeptide contained in host cells.

However, as will be set forth in detail below, Applicants submit that the methods defined by claims 1-3, 5-8 and 11-20 are not anticipated by Builder et al. Accordingly, this rejection is traversed, and reconsideration is respectfully requested.

More particularly, according to claim 1, the invention is directed to a method for the production of recombinant peptides with a low amount of trisulfides. The method comprises fermenting cells to produce the recombinant peptides. A metal salt is added during or after the fermentation step, prior to peptide isolation.

Accordingly to claim 2, the invention is directed to a method for the reduction of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides. A metal salt is added during or after fermentation, prior to peptide isolation.

According to claim 20, the invention is directed to a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides. A metal salt is added during or after fermentation, prior to peptide isolation.

Builder et al disclose a method for increasing the yield of correct refolding of a misfolded polypeptide, specifically IGF-I, and reactivating misfolded IGF-I contained in host cells. While Builder et al disclose metal salts are provided in the fermentation medium, Applicants find no teaching, suggestion, or reference for reducing trisulfide formation in the production of recombinant peptides, as presently claimed. Builder et al only broadly assert that the medium may be "supplemented as necessary" with various components including, among others, salts (column 15, line 65--column 16, line 12). Applicants find no teaching, suggestion or reference for using a metal salt for reducing trisulfide formation in the production of recombinant peptides. Furthermore, IGF-I refers to insulin-like growth factor-I, which is not known to Applicants to produce trisulfides when the polypeptide is formed. Thus, the methods and polypeptide IGF-I of Builder et al do not inherently encompass and are distinct from the methods of the present invention.

Anticipation under 35 U.S.C. §102(e) requires the disclosure in a single prior art reference of each element of the claims under consideration, *Alco Standard Corp. v. TVA*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). In view of the failure of Builder et al to teach, suggest, or recognize methods for the production of recombinant peptides with a low amount of trisulfides, methods for the reduction of the amount of trisulfides in the production of recombinant peptides, and a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides, Builder et al do not disclose each element of the present claims, and therefore do not anticipate claims 1-3, 5-8 and 11-20 under 35 U.S.C. §102(e).

It is therefore submitted that the methods defined by present claims 1-3, 5-8 and 11-20 are not anticipated by Builder et al, and that the rejection under 35 U.S.C. §102(e) has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Examiner's rejections under 35 U.S.C. §§102 and 112, second paragraph, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,


Holly D. Kozlowski, Reg. No. 30,468
Attorney for Applicants
DINSMORE & SHOHL LLP
1900 Chemed Center
255 East Fifth Street
Cincinnati, Ohio 45202
(513) 977-8568

VERSION WITH MARKINGS SHOWING CHANGES MADE

In the Claims:

Claim 20 is amended to read as follows:

20. (Amended) Method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides, comprising fermenting cells to produce recombinant peptides, wherein a metal salt is added during or after fermentation, prior to peptide isolation.